PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Hideki ENDOH, et al.

Docket No: Q82704

Appln. No.: 10/502,279

Group Art Unit: Not yet assigned

Confirmation No.: Not yet assigned

Examiner: Not yet assigned

Filed: July 22, 2004

For: METHOD FOR SCREENING A DRUG AMELIORATING INSULIN RESISTANCE

SUBMISSION OF ENGLISH TRANSLATION OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Attached please find a copy of an English Translation of the International Preliminary Examination Report received from the Applicants, to advance prosecution in the event such is not readily available from the International Bureau. Claims 1-18 of the application were found to be novel, involve an inventive step and include industrial applicability.

Respectfully submitted,

Mark Boland
Registration No. 32,197

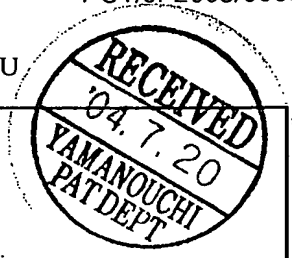
SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: October 26, 2004

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU



PCT

NOTIFICATION OF TRANSMITTAL OF COPIES OF TRANSLATION OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 72.2)

To:

NAGAI, Shozo
c/o Yamanouchi Pharmaceutical Co., Ltd.
Patent Department
17-1, Hasune 3-chome
Itabashi-ku, Tokyo 174-8612
JAPON

Date of mailing *(day/month/year)* 15 July 2004 (15.07.2004)	
Applicant's or agent's file reference Y0304-PCT	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2003/000546	International filing date *(day/month/year)* 22 January 2003 (22.01.2003)
Applicant YAMANOUCHI PHARMACEUTICAL CO., LTD. et al	

1. **Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. **Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, CO, EP, GH, KG, KR, MK, MZ, RO, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, BA, BB, BG, BR, BY, BZ, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, NO, NZ, OA, OM, PH, PL, PT, SC, SD, SE, SG, SK, SL, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 90 90

Translation

PCT Application
PCT/JP2003/000546

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Y0304-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/000546	International filing date (*day/month/year*) 22 January 2003 (22.01.2003)	Priority date (*day/month/year*) 23 January 2002 (23.01.2002)
International Patent Classification (IPC) or national classification and IPC C12N 15/12, 15/62, 15/81, C07K 14/705, 16/18, C12N 1/19, 1/21, A61P 3/10, C12Q 1/66		
Applicant YAMANOUCHI PHARMACEUTICAL CO., LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 09 June 2003 (09.06.2003)	Date of completion of this report 31 October 2003 (31.10.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/000546

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/00546

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claim No. 19

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claim No. 19 are so unclear that no meaningful opinion could be formed *(specify)*:

In looking at page 29, lines 2 to 9 of the Specification, it is entirely unclear which compounds are specifically included and which are excluded with respect to the "substance obtained by screening" in the description of the above claim. Therefore, the description of the above claim is exceedingly vague and no meaningful opinion can be rendered concerning this claim.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim No. 19.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/00546

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-18	YES
	Claims		NO
Inventive step (IS)	Claims	1-18	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

2. Citations and explanations

Document 1: EP 193256 A (Takeda Chemical Industries, Ltd.) September 3, 1986
Document 2: JP 2001-340080 A (Yoshitomo OKA) December 11, 2001 (Family: none)
Document 3: WO 99/12534 A1 (Ono Pharmaceutical Co., Ltd.) March 8, 1999
Document 4: TREUTER E. et al. A regulatory role for RIP140 in Nuclear receptor activation., Molecular endocrinology, 1998, Vol. 12, No. 6, p. 864-881
Document 5: EP 1057896 A1 (Tanabe Seiyaku Co., Ltd.) December 6, 2000
Document 6: EP 930299 A1 (Japan Tobacco Inc.) July 21, 1999
Document 7: WO 97/31907 A1 (GLAXO GROUP LTD) September 4, 1997

Document 1 describes the production of thiazolidine derivatives as medicines to treat diabetes mellitus.

Document 2 describes a screening method for medicines to treat insulin resistance that do not cause edema. In addition, it states that thiazolidine derivatives have the adverse reaction of causing edema, and that they increase the concentration of vascular endothelial growth factor in the blood of patients.

Document 3 states that thiazolidine derivatives are known as medicines to treat non-insulin dependent diabetes, i.e., as hypoglycemic agents, and that they show as medicines for the treatment of insulin resistance. It also states that one of the intracellular target proteins of thiazolidine derivatives is the PPARγ receptor, and it has been reported that thiazolidine derivatives increase the transcription activity of the PPARγ receptor, and that they increase the amount of body fat, and cause weight gain and obesity.

Document 4 states that it demonstrates that the ligand-dependent interaction between PPARγ and RIP 140 changes in a yeast two hybrid system.

Document 5 describes a method for screening for novel drugs that act on PPAR by measuring the ligand-dependent interaction between PPAR and transcription cofactors using a yeast two hybrid system.

Documents 6 and 7 describe compounds that are PPARγ agonists and compounds that are hypoglycemic agents. In addition, they are identical to the compounds described on page 31 of the Specification of this application as "primary ligands and secondary ligands."

However, documents 1-6 do not describe the screening for proteins that interact ligand-dependently with PPARγ, and no suggestions can be found elsewhere to search for such proteins.

As a result, the inventions of claims 1-18 are novel, involve an inventive step, and have industrial applicability.